REMARKS

Applicant has amended claim 1 to rephrase, and remove the objected to term "cloned". The applicant submits that the claim, as amended, clearly indicates that the fragments originate from polynucleic acid in coding llama antibodies.

Applicant has amended claims 5 and 6 with respect to claim dependency.

Applicant has amended claims 1 and 25 (upon which claims 2, 3, 8, 9, and 26 to 30 depend) to clarify and remove the objected to phrasing "said fragments comprising fragments...".

Claims 5 and 6 have been amended to remove the objected to phrasing "10^9 clones" and "10^8 clones". The applicant submits that these claims, as amended, when read by one skilled art would be clearly understood to refer to the number of different fragments represented in the library.

Claim 25 (upon which claims 26 to 30 depend) has been amended to delete the objected to phrasing "conventional heavy chain" and replace it with VH. The applicant submits that one skilled in the art would readily understand what is intended.

Applicant submits that claims 1 to 3 and 5 to 9 are clear with respect to the required antigen-binding affinity. Applicant submits that one skilled in the art would readily understand that what is referred to is not binding to a particular antigen in all cases, but in fact binding affinity for <u>any</u> antigen. It is the ability to obtain useful binding affinities from a naïve source (thereby permitting use for a range of possible antigens, rather than strictly what was immunized for as would be the case in a different situation) that could motivate one to employ the disclosure of the invention.

35U.S.C.102(b) Objection – Casterman *et al*

The claims of the present invention are directed to phage display libraries in phage vectors. Casterman discloses the use of phagemid vectors, rather than phage vectors.

This distinction is very important, as the use of phage vectors, and not phagemid vectors, is a practical necessity in the production of a library, as claimed, comprising fragments with a useful binding affinity for antigen. Details of the reasons for this can be found in the attached Declarations of Arumugam Muruganandam and Jamshid Tanha. In brief, phagemid vectors are not a multivalent display system, as a phage vector is. This multivalency is necessary to generate good binding from an inherently low affinity source such as a non-immunized animal.

In addition, Casterman fails utterly in teaching how one would produce a display library from a non-immunized source. One skilled in the art at the time, had they even believed it was possible to produce such a library in light of the Casterman reference, would have ordinarily used a phagemid vector, and would therefore not be expected to succeed. This is further detailed on page 2 of the Declaration of Arumugam Muruganandam. In addition, the Declaration of Jamshid Tanha, also attached as part of this Response, describes the results of an experiment he conducted producing in parallel, libraries using phage vectors or phagemid vectors, and revealing that while the phage vector library gave useful binding fragments, the phagemid vector library failed to do so

Thus, the applicant submits that Casterman fails to disclose and fails to teach how to produce, a display library producing fragments having a useful binding affinity.

35U.S.C.102(e) – Frenken *et al - A and B*

The references of Frenken refer to the use of phagemid vectors, not phage vectors. As discussed above, this distinction is very important, and distinguishes the present invention from the cited art.

The attached Declarations of Arumugam Muruganandam and Jamshid Tanha describe why the use of a phagemid vector, as disclosed in the references of Frenken, would not provide a library as claimed in the present invention.

35U.S.C.103(a)

The claims, as amended, are directed to libraries derived from phage vectors. For the reasons discussed above, and proved in evidence in the attached Declarations of Arumugam Muruganandam and Jamshid Tanha, neither the reference of Casterman, nor either of the references of Frenken, could provide or even lead one in the direction of the invention, as neither suggests the use of phage vectors.

One skilled in the art would have employed phagemid vectors, and therefore have been expected to fail in producing a library having fragments with useful binding affinities. The cited references would not be sufficient to direct one towards the use of phage vectors, which would have been a practical necessity to achieve the library claimed herein.

Applicant has rewritten cancelled claim 4, to delete the text of this claim, as referred to in the most recent Office Action.

This Response is being filed within two months of the mailing date of the Final Action, and an Advisory Action is thus respectfully requested, should the Examiner find any outstanding issues in relation to this application and claims.

Should the Examiner feel that any outstanding issues remain, he is also respectfully invited to telephone the undersigned at the number indicated.

Prompt and favorable action is respectfully requested.

Respectfully submitted,

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CERTIFICATE OF FACSIMILE TRANSMISSION

I hereby certify that this paper is being facsimile transmitted to the Patent and Trademark Office on the date shown below.

Margaret McKay — January 14, 2005